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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/643,683 | 08/18/2003 | James Robert Swartz | STAN-273 | 4598 |

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EXAMINER

VOGEL, NANCY S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1636

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/643,683 | Applicant(s) SWARTZ ET AL. | |
| | Examiner Nancy T. Vogel | Art Unit 1636 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 21 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 21 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>1/9/04</u> | 6) <input type="checkbox"/> Other: ____ |

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DETAILED ACTION

Claims 1-13 and 21 are pending in the case

Receipt of the Information Disclosure statement on 1/9/04 is acknowledged.

Election/Restrictions

Applicant's election of Group I, claims 1-13 and 21 in the reply filed on 2/1/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, it is noted that Applicant has cancelled non-elected claims 14-20.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (J. Biotechnol., 84, 27-32, 2000).

Kim et al. disclose a method for enhanced synthesis of biological macromolecules which are polypeptides *in vitro*, the method comprising synthesizing said biological macromolecules in a reaction mix which comprises an extract from *E.*

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coli grown in glucose and phosphate containing medium, and wherein said reaction mix comprises magnesium at a concentration of 16 mM (see page 28, paragraph bridging first and second column). Since the conditions are the same as those set forth in the instant specification (page 4), it is considered that the reaction mix has activated oxidative phosphorylation.

Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by Alakhov et al. (US Patent 5,478,730), or Baranov et al. (Methods in Enzymology, 217, 123-142, 1993).

Alakhov et al. and Baranov et al. each disclose a method for in vitro synthesis of properly folded polypeptides comprising synthesizing said polypeptide in a reaction mix substantially free of polyethylene glycol (see column 7, lines 40-50, column 8 lines 14-25 of Alakhov et al.; see Table 1, Experiment 5 conditions, and page 136 Experiment 5 of Baranov et al.). Therefore any benefit set forth in the claim (ie. "enhanced in vitro synthesis of properly folded polypeptides") is inherent in the method disclosed by Alakhov et al. or Baranov et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 1-13 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. in view of Baranov et al. (Methods in Enzymology, 217, 123-142, 1993).

Kim et al. is cited essentially for the reasons set forth above.

The difference between the reference and the instant claim is that the synthesis of biological macromolecules is performed as a continuous reaction, and the reaction mix is substantially free of polyethylene glycol and comprises spermine, spermidine or putrescine. However, Baranov et al. disclose a method of synthesis of biological macromolecules (polypeptides) wherein said synthesis is performed as a continuous reaction. Baranov et al. disclose that such culture conditions allow constant activity for many hours, and result in preparative yields of protein products (paragraph bridging pages 123 and 124). Further, Baranov et al. disclose a method of in vitro synthesis of biological macromolecules in using reaction mixes which are substantially free of polyethylene glycol and which comprise spermidine and magnesium (see Table 1, Experiment 5 conditions, and page 136 Experiment 5). It would have been obvious to one of ordinary skill in the art to have modified the method of synthesis of polypeptides disclosed by Kim et al. by using continuous culture techniques and conditions as disclosed by Baranov et al., since both references are concerned with methods of producing maximal amounts of polypeptides using cell free expression systems made from E. coli extracts. One would have been motivated to do so by the well known advantages of continuous culture techniques, which include longer periods of activity (synthesis) and high yields of product, as disclosed by Baranov et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 1 is drawn to a method of synthesis of any biological macromolecule in vitro comprising synthesizing said biological macromolecules in a reaction mix where oxidative phosphorylation is activated. The specification does not provide a definition for "biological macromolecules", and therefore the broadest reasonable definition, i.e. any macromolecule present in a biological system, is assumed. Applicants have not provided a definition of the phrase "a reaction mix where oxidative phosphorylation is activated", but have described such a reaction mix as being one in which no secondary energy source is needed (page 6). Claims 1, 6-12 are genus claims in terms of a method of synthesizing any biological macromolecule in vitro. Claims 1-7 are genus claims in terms of a method of synthesizing a biological macromolecule, which may be

polypeptides or mRNA, using a reaction mix where oxidative phosphorylation is activated by any means.

The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods of synthesizing any biological macromolecules, or using any reaction mix where oxidative phosphorylation is activated. While the specification provides general information on producing mRNA and polypeptides in and in vitro cell-free expression system, there is no disclosure of the components or conditions necessary for the production of any other type of biological macromolecule. Furthermore, while the specification describes the reaction mix prepared from *E. coli* grown under specific conditions, which result in activated oxidative phosphorylation, there is no disclosure of any other types of reaction mixes having this property, or guidance regarding the identity of such reaction mixes. Therefore, the specification does not describe the claimed method of synthesis of biological macromolecules, using reaction mixes where oxidative phosphorylation is activated, in such full, clear, concise and exact terms so as to indicate that Applicant has possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of "enhanced", since it is not known to what the claimed method is being compared.

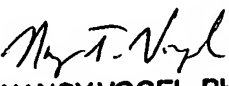
Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


NANCY VOGEL, PH.D.
PATENT EXAMINER